New Genomic Tests May Guide Choice Of Chemotherapy In Cancer Patients

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New Genomic Tests Guide Choice Of Chemotherapy In Cancer Patients

Scientists at Duke University's Institute for Genome Sciences & Policy have developed a panel of genomic tests that analyzes the unique molecular traits of a cancerous tumor and determines which chemotherapy will most aggressively attack that patient's cancer.

The tests work by scanning thousands of genes from a patient's tumor to produce a "genomic" profile of the tumor's molecular makeup, giving physicians a tool to match the right chemotherapy for the patient's tumor type. (Credit: Duke University Medical Center)

In experiments reported in the November 2006 issue of the journal Nature Medicine, the researchers applied the genomic tests to cells derived from tumors of cancer patients. They found that the tests were 80 percent accurate in predicting which drugs would be most effective in killing the tumor.

The Duke team plans to begin a clinical trial of the genomic tests in breast cancer patients next year.

The new tests have the potential to save lives and reduce patients' exposure to the toxic side effects of chemotherapy, said Anil Potti, M.D., the study's lead investigator and an assistant professor of medicine in the Duke Institute for Genome Sciences & Policy. The tests are designed to help doctors select and initiate treatment with the best drug for a patient's tumor instead of trying various drugs in succession until the right one is found, Potti said.

"Over 400,000 patients in the United States are treated with chemotherapy each year, without a firm basis for which drug they receive," said Joseph Nevins, Ph.D., the study's senior investigator and a professor of genetics at the Duke Institute for Genome Sciences & Policy. "We believe these genomic tests have the potential to revolutionize cancer care by identifying the right drug for each individual patient."

The tests work by scanning thousands of genes from a patient's tumor to produce a "genomic" profile of the tumor's molecular makeup. Using the genomic tests in cancer cells in the laboratory, the scientists successfully matched the right chemotherapy for the patient's tumor type. The scientists were then able to validate their predictions against patients' actual clinical outcomes.

Doctors currently must use a trial−and−error approach to chemotherapy, trying various established drugs to see which has an effect. As a result, patients often undergo multiple toxic therapies in a process that places patients' lives at risk as their conditions worsen with each treatment.

"Chemotherapy will likely continue to be the backbone of many anticancer treatment strategies," said Potti. "With the new test, we think that physicians will be able to personalize chemotherapy in a way that should improve outcomes."

The first clinical trial will compare how well patients respond to chemotherapy when it is guided by the new genomic predictors versus when it is selected by physicians in the usual trial−and−error manner. The researchers anticipate that they will enroll approximately 120 patients with breast cancer in the study. Subsequent clinical trials will enroll hundreds of patients with lung and ovarian cancer, Potti said.

If proven effective, the tests could be applied to all cancers in which chemotherapy is given, not just breast, lung, and ovarian cancer, Potti said.

The researchers developed the new tests through a process that included analyzing the activity of thousands of genes in cells taken from the tumors of cancer patients.

In using the test, scientists extract the genetic molecule "messenger RNA" from a cancer patient's tumor cells. Messenger RNA translates a gene's DNA code into proteins that run the cell's activities. Hence, it is a barometer of a gene's activity level inside the cell.

The scientists then label the messenger RNA with fluorescent tags and place the labeled molecules on a tiny glass slide, called a gene chip, which binds to segments of DNA representing the tens of thousands of genes in the genome.

When scanned with special light, the fluorescent RNA emits a telltale luminescence that demonstrates how much RNA is present on the chip, and this reading indicates which genes are most active in a given tumor. The scientists use this signature of gene expression in the cancer cells to predict which chemotherapeutic agent will be most powerful in treating the specific tumor.

In the current study, funded by the National Institutes of Health, the researchers assessed the tests' ability to predict how patients with

breast and ovarian cancer and leukemia responded to various anticancer drugs.

They found that the tests predicted the clinical response to chemotherapy with 80 percent accuracy.

"Importantly, we believe this research can improve the efficiency of chemotherapy without changing the drugs currently used in standard practice," Nevins said. "Rather, the tests simply provide an approach to better selection, within a repertoire of available drugs."

Other researchers participating in the study included Holly K. Dressman, Andrea Bild, Jeffrey Marks, Andrew Berchuck, Geoffrey S. Ginsburg and Phillip Febbo of the Duke Institute for Genome Sciences & Policy; Richard F. Riedel, Robyn Sayer, Janiel Cragun, Michael J. Kelley, Rebecca Peterson, and David Harpole of Duke University Medical Center; and Gina Chan, Hope Cottrill and Johnathan Lancaster of the H. Lee Moffitt Cancer Center in Tampa, Fl.

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